Site: Syntex-Verona
ID#: MOD007452154 3/16-17/71
Break: 1.6 H.W.S.
Other:
3-16-71

EIR
Hoffman-Taff, Inc.
Springfield, Missouri

SUMMARY OF FINDINGS:

Inspection of this firm 1/5/65 was classified as violative due to questionable labeling and poor controls, and resulted in Notice of Hearing being issued to the firm 5/19/65, regarding 016-543 B, Betaine Hydrochloride. Inspection of 1/18/66 was violative due to lack of controls and continued label discrepancies. Follow-up samples were classified as being in compliance. The inspection of 8/29/67 revealed minor GMP deviations. Inspections of 4/15/69 and 5/7-8&11/70 revealed minor control weaknesses. During both of these inspections, it was noted that the label of the product, Chloral Betaine lacked the prescription drug legend. This product is a control drug. Additionally, the booklet, "Choline--Its Applications in Medicine and Nutrition," appeared to make excessive claims for Choline products. Choline is manufactured by the Hoffman-Taff plant at Verona, but labeling is the responsibility of the Springfield home office. Following the last inspection, Kansas City Field Office requested DCG review of promotional material. Based on the DCG review, a letter was issued to the firm 2/12/71, advising them that the Choline booklet and various product information sheets are considered labeling, and therefore must comply with Regulation 1.106(b)(4)(i) for human use or 1.106(c)(4)(i) for veterinary use.

Current inspection reveals that the firm continues to manufacture bulk drugs and vitamins. Controls in general are satisfactory. Labels for Chloral Betaine lack the prescription legend. The firm has not yet changed or discontinued the use of promotional literature referred to in the February, 1971, letter.
Control weaknesses pointed out during the last inspection have been corrected.

HISTORY OF BUSINESS:

Hoffman-Taff, Inc., is a subsidiary of Syntex Laboratories, Inc., Palo Alto, California. Corporate officers remain the same as reported during the 5/7-8&11/70 inspection. Hoffman-Taff, Inc., operates as a separate corporation, with the main office at Springfield, Missouri.

The Springfield plant manufactures bulk drugs and vitamins in the following categories: Prescription, non-prescription, pharmaceutical, and feed-grade. The firm is registered for 1971 in accordance with Section 510 of the Act.

PERSONS INTERVIEWED:

Credentials were shown and a completed Notice of Inspection was presented to Mr. William John Zay, Plant Manager. Mr. Zay accompanied me on the inspection of the manufacturing plant and control laboratory, and

furnished all information requested during that part of the inspection. He instructed the firm's supervisors to explain production details of their respective departments.

During coverage of the control laboratory, Mr. William Zay requested that Andrew Zay, Senior Analyst, explain the operation of the laboratory. Andrew Zay was in charge of the laboratory in the absence of Mr. Walter R. Friedhofen, Director of Quality Control.

Mrs. Pat Garoutte is in charge of label issuance at the plant. She explained procedures and supplied me with copies of the product labels.

Mr. Maxwell L. Cooley, Manager of Technical Sales Service, located in the main office of Hoffman-Taff, supplied copies of promotional material and information on label printing.

INDIVIDUAL RESPONSIBILITY:

Mr. William J. Zay, Plant Manager, stated he was responsible for day-to-day operation of the manufacturing plant. Production supervisors are responsible to Mr. Zay. Mr. Zay stated he is in turn responsible to Mr. Godfrey J. Moll, Vice-President in Charge of Production. Mr. Moll is responsible to Mr. James J. Rattray, President of Hoffman-Taff, Inc.

Mr. Walter R. Friedhofen, Laboratory Director, is responsible for the operation of the control laboratory, and signs all certificates of analysis sent to customers. Mr. Friedhofen was not present during the inspection. Mr. Zay stated Mr. Friedhofen is responsible to Mr. E. Barkley, Executive Vice-President of Hoffman-Taff, and Mr. Rattray, President of Hoffman-Taff.

Mr. Maxwell Cooley, Manager of Technical Sales Service, stated he was responsible for label copy and all promotional literature. Mr. Cooley's office is located at the main office, 1915 W. Sunshine, Springfield, Missouri. Mr. Cooley stated he was presently responsible to Mr. Eddie Bass, Vice-President of Sales. Mr. Cooley stated he will soon assume different responsibilities in the area of animal nutrition.

GUARANTEES AND LABELING AGREEMENTS:

Neither Mr. William Zay nor Mr. Maxwell Cooley were aware of guarantees, but they stated customer specifications are on file and must be met for each product. Mr. Friedhofen signs a certificate of analysis which is sent to the customer with each shipment. Raw-material specifications have been established with all raw-material suppliers.

RAW MATERIALS:

Most raw materials utilized are bulk liquids received by either truck or railcar. Storage of these items is in large storage tanks. Raw-material handling and controls remain the same as previously reported; handling appears to be satisfactory.

EQUIPMENT AND PROCESSES:

The manufacture of this firm's bulk drugs involves a series of chemical reactions taking place in large reactors. Temperature in reactors is controlled to either speed up or slow down the reactions. Liquid ingredients are metered into the reactors. Products are generally transfered by pumping or gravity flow. One or more purification steps are usually involved. Drying is accomplished with roller driers.

All equipment is identified by number, and is recorded in the production records. Run numbers are used to identify in-process materials. Production controls remain the same as previously reported, and appear to be satisfactory. Each reactor is equipped with a recording thermometer--the charts of which are retained with the production records. Mr. Zay stated the temperature charts are considered quite important, as they indicate the addition of ingredients in various stages of a reaction.

Finished products are packaged in Poly-lined drums or Poly-lined paper bags. During packaging, the final samples for the laboratory are taken by production personnel. Packaged products are quarantined pending sample analysis. Finished products are stored unlabeled, identified by the run number, and product name. Product identification and handling appears satisfactory.

Products are not labeled until an order has been received and a shipping order made out. At this time, labels are requested by completion of a label requisition form. This form goes to Mrs. Pat Garoutte, Label Inventory Clerk, who issues an exact number of labels. She types in such information as lot numbers, weights, etc., onto the labels. The labels are returned to the shipping department with a copy of the requisition form. Labels are stored in locked drawers with only one type of label per drawer. Mrs. Garoutte maintains a label log-book listing all label transactions. An actual inventory is not kept. Label requisitions were not kept by Mrs. Garoutte. Labels and literature are printed by Roberts & Sutter Printers, Inc., Springfield, Missouri.

LABORATORY CONTROLS:

The control laboratory at the Springfield plant also does analytical work for the Verona plant. Most analyses are performed by technicians under the direction of Mr. Walter Friedhofen or Mr. Andrew Zay. Product specifications have been established for all finished products. Each batch is tested, and most products are subjected to one or more in-process tests. One chemist does all gas chromatography work on a Barber-Coleman Model #5300. Very little gas chromatography work is currently done, but the firm has on order a Tracor MT-220, which will reportedly permit much more testing by this method, including raw-material testing, which is now done only occasionally. A biological laboratory has been established for testing antibiotic feed premixes, among other things.

Test procedures are N.F., U.S.P., or A.O.A.C., where applicable. All calculations, etc., are checked by Mr. Friedhofen or Mr. Andrew Zay. Mr. Friedhofen issues certificates of analysis for each product in each shipment. Reserve samples are retained five years. Sample-handling and general laboratory operations appear satisfactory.

MANUFACTURING CODES:

Lot numbers are assigned by quality control after a batch has been passed. The lot numbers are consecutive numbers for the batches of each product prefixed by letters designating the product.

DISCUSSION WITH MANAGEMENT:

Most discussion during the inspection with Mr. William Zay, Plant Manager, concerned obtaining information contained elsewhere in this report. We discussed the firm's production control system in some detail. I made no specific recommendations. The production control system is rather complex, and control records are maintained at various locations.

Discussion with Mr. Andrew Zay concerned only obtaining information on the operation of the laboratory.

After completing the inspection of the plant and laboratory, Mr. William Zay arranged for me to meet with Mr. Maxwell Cooley at the main office to discuss labeling and promotional material. Mr. Cooler stated he had received Dr. Kramer's letter of 2/12/71, but had not yet had an opportunity to answer the letter. The various product information sheets and booklet on Cholines remain in the storage area in the basement

of the office building. Mr. Cooley and I briefly discussed the problem of devising adequate product information sheets. I told Mr. Cooley I felt the product information sheet was primarily a specification sheet, and he could possibly satisfy the requirements of full disclosure by omitting uses from the sheets. I told Mr. Cooley that this was just my opinion, and he should check with the District Office for more specific information. Mr. Cooley stated he thought the firm would use the remainder of the present supply of product information sheets and Choline booklets before making any changes. I advised Mr. Cooley to contact the District Office when he made his final decision.

I once again pointed out to Mr. Cooley that the labels for Chloral Betaine lacked the prescription legend. He stated he thought the labels had been corrected following the last inspection. He stated he would have the legend placed on the next printing, and would have it typed on the current stock of labels.

DISTRIBUTION:

Distribution is nationwide via common-carrier or the firm's own fleet of trucks. Most products are handled at the following warehouses:

1. Daview Warehouse Co., 164 So. Central Ave., Los Angeles, Calif.

2. Raymond Peters Hoffman Laboratories, 459 E. First Ave., Roselle, N.J.

Most of the Chloral Betaine is sold to Meade-Johnson Co., Evansville, Indiana. No specific shipments were obtained.

Distribution records are maintained in a manner which would facilitate recall if ever necessary.

EXHIBITS:

Submitted with this report are the following exhibits: Copies of all specification sheets, a 60-page booklet on Pantothenic Acid and its derivatives, pharmaceutical product list, copies of representative labeling, a 51-page booklet entitled, "Choline--Its Application in Medicine and Nutrition."

HWS:rpp
4/5/71

Herbert W. Smith, 226
Inspector